REMARKS

Reconsideration and withdrawal of the claim rejections are requested in view of the amendments and remarks herein. The Examiner is thanked for indicating that claims 28, 29, 35 and 36 are free of the prior art.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1-5, 7-21, 26, 27 and 29-42 are pending in this application. Claims 1, 2, 9, 12, 13, 26, 27 and 34 are amended; claims 6, 22-25 and 28 have been cancelled.

Support for the amended claims is found throughout the specification. Specifically, support for the hybridization conditions in claims 1 and 2 can be found on page 14, lines 3-7 of the application. Support for the recitation of "100 nucleotides in length", in claims 27 and 34, can be found on page 20, line 34. The remaining amendments are related to form only, and do not affect the scope of the claims. No new matter is added.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and that these claims are and were in full compliance with the requirements of 35 U.S.C. §112. The amendments of and additions to the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the herewith amendments should not give rise to any estoppel, as the herewith amendments are not narrowing amendments.

II. THE REJECTIONS UNDER 35 U.S.C. §112, 1ST PARAGRAPH ARE OVERCOME

The Application Contains Adequate Written Description

Claims 1-5, 7-21, 24 and 26-42 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking adequate written description. The rejection is traversed.

Claims 1 and 2 have been amended to recite specific hybridization buffer and temperature conditions. It should be noted that page 14 of the present specification teaches two different hybridization buffers, usable alternatively. The first contains 2X SSC, while the second contains 7% SDS. These conditions, and a hybridization temperature of 68°C, are recited in claims 1 and 2; therefore, the claims should meet the written description requirement.

Applicants maintain that there is adequate written description for the recitation of percent sequence identity in claim 1, and direct the Examiner's attention to Example 14 of the USPTO's

"Synopsis of Application of Written Description Guidelines". Example 14 presents a fact pattern that is analogous with that of the instant application. The claim in Example 14 recites (1) the structure of the claimed protein, in the form of a SEQ ID NO and variants with a particular percent identity to the recited sequence, and (2) function, in the form of identifying the reaction that the protein catalyzes (*i.e.* its enzymatic activity). Claim 1 of the instant application recites (1) structure of the claimed protein in the form of a SEQ ID NO, and variants having at least about 85% identity with the nucleic acid molecule encoding the claimed protein and (2) function of the claimed protein in the form of its β-amylase activity. Methods for analyzing starch (and thus assessing β-amylase activity) produced by transgenic plants expressing SEQ ID NO:2 are provided in the application, beginning on page 39, and are standard in the art. As discussed in Example 14, even if the claimed SEQ ID NO is the only species disclosed, it is representative of the genus because all members of the genus have the claimed level of identity with, and function of, the protein described by the reference sequence. Accordingly, it is submitted that the claims meet the written description requirement.

The Claims Are Enabled

Claims 1-5, 7-21, 24 and 26-42 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. The rejection is traversed.

Applicants reiterate that there would be no undue experimentation on the part of the skilled artisan to isolate the claimed nucleic acid molecules. The Court of Appeals for the Federal Circuit in the case of *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988):

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. **The key word is undue, not experimentation.** The determination of what constitutes undue experimentation in a given case requires the application of standard of reasonableness, having due regard for the nature of the invention and the state of the art. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed ... [Emphasis added. Citations omitted].

Id. at 1404.

Against this background, determining whether undue experimentation is required to practice a claimed invention turns on weighing many factors summarized in *In re Wands* (*Id.*),

for example, (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples of the invention; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims.

Applying *Wands* to the instant facts, enablement is shown to exist. The fact that some experimentation may be required does not mean that it is undue. The amount of direction or guidance presented is high. Applicants have provided nucleic acid and amino acid sequences, and functional assays, for β-amylase. The synthesis or isolation of nucleic acid molecules encoding polypeptides with a high degree of homology to SEQ ID NO:2 is routine. The relative skill of those in the art is high.

As to the predictability of the art, Applicants dispute the Examiner's assertion that Kossmann *et al.* and Willmitzer *et al.* teach that altering starch biosynthesis is unpredictable. Willmitzer *et al.* describes the down-regulation of a branching enzyme in potato. It was mere speculation that starch would be altered by down-regulation of a specific branching enzyme. Willmitzer *et al.* also speculated the existence of a second isoform of branching enzyme in potato as the reason for failure to achieve the desired results (page 38, 5th paragraph). Later publications have demonstrated that this is indeed the case, and that the down-regulation of the second branching enzyme in potato does lead to the results that were expected by Willmitzer *et al.* Therefore, Willmitzer *et al.* were correct in predicting that, based on plant species which were already known to encode two different branching enzymes, potato plants were likely to have more than one isoform of branching enzyme as well (page 38, 3rd paragraph). Thus, Willmitzer *et al.* actually argues in favor of predictability, rather than against it.

In addition, Safford *et al.* (Carbohydrate Polymers 35, 1998, 155-168; copy attached) showed that, by inhibiting the branching enzyme of Willmitzer *et al.* in potato, the amount of phosphate covalently bound to starch isolated from transgenic potato lines is elevated by 50-100% (page 159, left column, 2nd paragraph). The results of Safford *et al.* were not detected by Willmitzer *et al.* because they did not measure the phosphate content of starch. The increase of phosphate in starch isolated from the lines described by Willmitzer *et al.* is also described in Kossman *et al.* (page 278, 2nd paragraph).

Similarly, Kossmann *et al.* also does not support the allegation that the art is unpredictable. Lloyd *et al.* (Biochem. J. 338, 1999, 515-521, copy attached) clearly shows that

the plants described by Kossman *et al.* have an altered side chain distribution of amylopectin (page 518, 2nd column, 1st paragraph and page 513, 2nd column, last paragraph). It should be noted that the starch synthase called GBSS II (**G**ranule **B**ound **S**tarch **S**ynthase isoform II) in Kossman *et al.* was later renamed SS II or SSS II (**S**oluble **S**tarch **S**ynthase isoform II). According to Lloyd *et al.*, the misleading results obtained by Kossman *et al.*, were due to the analytical methods used by Kossman *et al.*, which do not enable the detection of the effects seen by Lloyd *et al.* (see Lloyd *et al.*, page 520, 1st paragraph of the discussion). Thus, that "... no difference in the chain length distribution using HPAE ... can be found" by Kossman *et al.* (see page 275, 6th paragraph) is due to the fact that the method used did not allow the detection of differences in chain length distribution. Kossman *et al.* did not say that there were no differences in side chain length distribution. Lloyd *et al.* later demonstrated that, by using different tools for analysis of starch isolated from the transgenic plants of Kossman *et al.*, altered side chain distribution is indeed recognizable. Although Lloyd *et al.* also used an HPAE-based method to perform their analysis, different separation columns and a different detection system enabled Lloyd *et al.* to obtain data that was not detected by Kossman *et al.* This clearly demonstrates that Kossman *et al.* cannot be used in support of unpredictability of the art because it relies on effects which did indeed exist, but were interpreted incorrectly when taken alone.

In addition, the Office Action argues that the specification does not give any guidance to make and use any particular fragment of SEQ ID NO: 1. Claim 27 has been amended to recite fragments of more than 100 nucleotides in length. A person skilled in the art is able to make antisense constructs for suppression of gene expression in plants, and would face no undue experimentation in doing so.

It is submitted that the claims are in compliance with the first paragraph of §112, and reconsideration and withdrawal of the rejections thereunder are requested.

III. THE REJECTIONS UNDER 35 U.S.C. §112, 2ND PARAGRAPH ARE OVERCOME

Claims 1-5, 7-21 and 24 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

Claims 1 and 2 were rejected for reciting "under stringent conditions", which recitation has been deleted from claim 1.

The language of claim 2 has been modified to clarify that the claimed recombinant nucleic acid molecule contains a) a nucleic acid molecule encoding a β-amylase and b) a nucleic

acid molecule encoding a protein involved in starch metabolism or a nucleic acid that hybridizes to a nucleic acid molecule encoding a protein involved in starch metabolism.

The dependence of claims 12 and 13 has been amended and claim 24 has been cancelled, obviating the rejection of those claims on the basis of improper dependence. The cancellation of claim 24 also obviates its rejection under 35 U.S.C. §101.

It is believed that the claims meet the requirements of 35 U.S.C. §112, second paragraph, and reconsideration and withdrawal of the rejections are requested.

IV. THE REJECTIONS UNDER 35 U.S.C. §102 ARE OVERCOME

Claims 1-5, 7-12, 24, 26, 27, 30-34 and 37-42 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Yoshida *et al.* ("Yoshida 1"). The rejection is traversed.

Yoshida 1 relates to sweet potato β-amylase, the sequence of which was published in Yoshida *et al.*, 1992, Gene 120 ("Yoshida 2") or as EMBL Accession No. D12882. Initially, it is noted that neither Yoshida 1 nor Yoshida 2 relates to potato β-amylase, as is recited in the present claims, but to sweet potato β-amylase, which is an entirely different plant and molecule.

As demonstrated in the Amendment filed on June 2, 2003, the sequence identity between the β-amylase of Yoshida *et al.* and that of the present invention is only 54.9%. The Office Action appears to argue that the hybridization conditions previously recited in the claims would yield the sequence of Yoshida *et al.* It is submitted that the hybridization conditions, as currently recited, would not yield the sweet potato β-amylase of Yoshida *et al.*, and clearly place sweet potato β-amylase outside of the scope of the instant claims.

Further, claim 27 now recites a nucleic acid sequence of at least about 100 nucleotides, rendering the sequence overlap between Yoshida *et al.* and the molecule of the instant invention at positions 934-949 moot.

Claims 27, 30-34 and 37-42 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Sadowski *et al.* The rejection is traversed. Claim 27 now recites a nucleic acid sequence of at least about 100 nucleotides, and as the fragments of claim 34 are also specified to be at least about 100 nucleotides in length, obviated the rejection over Sadowski *et al.*

Therefore, the subject matter of the present invention is clearly novel over the cited references, and reconsideration and withdrawal of the rejection under 35 U.S.C. §102 are requested.

V. THE REJECTION UNDER 35 U.S.C. §103 IS OVERCOME

Claims 1-5, 7-21 and 24 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Taylor *et al.* in view of Yoshida *et al.* ("Yoshida 1"). The rejection is traversed.

As discussed above and in the Amendment filed on June 2, 2003, the teachings of Yoshida *et al.* are distinct from those of the instant invention, as it does not teach or suggest a nucleic acid molecule with the sequence of SEQ ID NO:1, or a nucleic acid molecule with at least 85% sequence identity to SEQ ID NO:1, or a nucleic acid molecule which encodes a protein with the sequence of SEQ ID NO:2. In view of the low degree of sequence identity and the distribution of identical nucleotide positions between Applicants' sequence and Yoshida's sequence, the skilled artisan would not have been able to arrive at the instant invention with or without Taylor *et al.*

Applicants apologize for any confusion created in the June 2, 2003 Amendment with respect to the discussion of Yoshida *et al.* The passages and page numbers referred to were from Yoshida 2, rather than Yoshida 1, which was the document cited in the Office Action. However, Yoshida 2 relates to the same molecule as discussed in Yoshida 1; therefore, the teachings therein and Applicants' discussion thereof are still relevant. Yoshida *et al.*

As discussed above, the enzyme of Yoshida *et al.* is entirely different than that of the current invention, and shares only about 55% sequence identity with the claimed β-amylase from potato. These deficiencies are not cured by Taylor *et al.*, which relates to an entirely different protein, α-glucosidase. The mere existence in potato of <u>other</u> enzymes involved in starch metabolism in no way makes the discovery of potato β-amylase obvious. Even if one of skill in the art might have speculated that potatoes contain β-amylase, no teachings as to the structure of potato β-amylase were available prior to the instant invention. Given the low degree of homology between β-amylases from different plants (according to the abstract of Yoshida 1, sweet potato, barley and soybean β-amylases share only about 68% identity), the skilled artisan could not have envisioned the currently claimed molecule based on the teachings of Yoshida *et al.*, with or without the teachings of Taylor *et al.*

As neither Yoshida *et al.* nor Taylor *et al.*, alone or in combination, teach or suggest the instant invention, reconsideration and withdrawal of the rejection under 35 U.S.C. §103 are requested.

CONCLUSION

In view of the remarks and amendments herewith, it is believed that the application is in condition for allowance, or at least in better condition for appeal. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP
Attorneys for Applicants

By: 

Marilyn Matthes Brogan
Registration No. 31,223

Anne-Marie C. Yvon, Ph.D.
Registration No. 52,390
(212) 588-0800